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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/625,963	07/26/2000	Hans Josef Stauss	ICI 101	8595

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EXAMINER	
VANDERVEGT, FRANCOIS P	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/625,963	STAUSS ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication app ars on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2003 and 10 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5,7,15 and 19* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5,7,15 and 19* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11052003*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

The Examiner in charge of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to F. Pierre VanderVegt, Ph.D. in Art Unit 1644.

Claims 2-4, 6, 8-14, 16-18, 20-43 and 45-48 were previously canceled.

Claim 44 has been newly canceled.

Claims 1, 5, 7, 15 and 19 are currently pending and are the subject of examination in the present Office Action.

In view of Applicant's amendment filed November 5, 2003 only the following ground of rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 15 and 19 stand rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It was previously stated: "The instant claims are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for the recitation of a vaccine for any tumor cell, including those that over express WT-1. Neither does the instant specification provide enablement for how to make and use a peptide having at least nine but fewer than 100 amino acids, comprising the amino acid sequence of SEQ ID NO: 1, (RMFPNAPYL), a pharmaceutical composition thereof, and a vaccine comprising said peptide, wherein said peptide is capable of binding to HLA-A0201 or is capable of being processed by an antigen presenting cell so that a fragment is produced which is able to bind HLA-A201, other than a peptide consisting of SEQ ID NO:1 itself.

As such, the specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed in the instant claims without an undue amount of experimentation. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of peptides broadly encompassed by the claims, nor with the large number of tumors.

The instant specification discloses cancers such as some leukemias that over express WT-1 (comprising SEQ ID NO: 1), which the instant specification discloses as being derived from human WT-

1 transcription factor. The instant specification also discloses on page 54 and in Figures 5 & 6, that the peptide consisting of SEQ ID NO: 1 is, i) presented by leukemic tumor cell lines that over express WT-1 and express HLA-A2, ii) that CTL directed to the peptide consisting of the amino acid sequence of SEQ ID NO: 1 recognize CD34+ cells from HLA-A0201+ CML patients, as well as CD34+, HLA-A2+ leukemic tumor cell lines.

The instant specification provides insufficient guidance and direction that the recited peptides would be effective as a vaccine against any tumor, including those that over express WT-1 and that express HLA-A2.

The instant specification discloses in Figures 5 and 6 that a peptide of SEQ ID NO: 1 is effective in killing cancer cells in vitro, but there is insufficient guidance from the instant disclosure on how to extrapolate from in vitro killing to in vivo killing.

Pages 53-54 disclose that the critical transformation events in CML and AML affect CD34+ cells, and that the in addition to the hallmark t(9;22) chromosomal translocation, the Wt-1 transcription factor is a candidate protein contributing to leukemogenesis, especially in view of its increased expression in CD34+ cells from CML and AML patients and in view of studies showing the in vitro enhancement of proliferation of hematopoietic cells with increased WT-1 expression, and that a recent study suggesting T cells specific for CD34+ progenitor cells are critically important in mediating anti-leukemic effects in CML patients.

However, Janeway teaches that melanoma tumor specific antigens which were recognized by CTL in vitro, were not expanded in vivo, suggesting that said peptides are not immunogenic in vivo (see page 551 of Janeway et al Immunobiology 4th Edition). Therefore, the in vitro data of the instant specification do not provide sufficient guidance and direction to extrapolate that a peptide comprising or consisting of SEQ ID NO: 1 is immunogenic in vivo and would be effective as a cancer vaccine, absent evidence to the contrary.

In view of the insufficient guidance and direction from the instant specification and in the art, with regard to the efficacy of the recited peptide, including a peptide consisting of SEQ ID NO: 1, as a tumor vaccine, it would require undue experimentation by one of skill in the art to develop a vaccine comprising a peptide comprising SEQ ID NO: 1, that would be effective in as a vaccine against any tumor, including tumors that over express WT-1, comprising the use of a peptide consisting of or comprising SEQ ID NO: 1."

Applicant's arguments filed November 5, 2003 have been fully considered but they are not persuasive. Applicant has submitted an evidentiary reference by Oka et al (J. Immunol. [2000] 164(4): 1873-1880; U1 on form PTO-892). Applicant contends that the Oka reference demonstrates that use of the presently claimed peptide as a vaccine is enabled. The Examiner respectfully disagrees with Applicant's position. The Oka reference discloses that CTL were induced *in vivo* that could recognize and kill WT1+ target cells *in vitro* (Figure 1 for example) by immunization with the RMFPNAPYL peptide. The Oka reference further shows that prophylactic administration of the RMFPNAPYL peptide induced the rejection of a WT1+ tumor challenge (Figure 6 in particular). However, neither the Oka reference nor the instant specification discloses the *in vivo* effectiveness of RMFPNAPYL peptide administration to a subject with an existing WT1+ tumor. Furthermore, effectiveness of the peptide against an *in* vivo tumor was shown only prophylactically in experimental animals that were administered tumor cells 3 weeks later. Accordingly, Oka was aware of which subjects should develop *in vivo* tumors.

However, the instant specification provides no means for predicting which subjects are to develop a WT1+ tumor and therefore would benefit from a prophylactic treatment with the RMFPNAPYL peptide. As a further point, the Oka reference's teaching of immunization with the RMFPNAPYL peptide does not enable for vaccine peptides of lengths greater than the peptide itself because the binding pockets of MHC class I molecules are closed and cannot accommodate peptides of greater than 12 amino acid residues in length. Accordingly, it is maintained that the instant specification lacks sufficient guidance and direction in regard to the efficacy of the recited peptide as a vaccine preparation. Claim 15 is included because recitation of a "pharmaceutical" composition in claim indicates that the composition is intended for administration to a subject, rendering the composition indistinguishable from the recitation of "vaccine" in claim 19.

The following represents a NEW ground of rejection and necessitate that this Office Action be made NON-FINAL.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

2. Claims 1, 5, 7, 15 and 19 are rejected under 35 U.S.C. 102(e) as being anticipated by the U.S. Patent Application Publication 20030082196 A1 (published May 1, 2003; on form PTO-892), which claims priority to U.S. Patent Application serial number 09/164,223; filed September 30, 1998.

The '196 publication teaches the RMFPNAPYL peptide of instant SEQ ID NO: 1 as an immunogenic fragment of the human WT1 polypeptide as SEQ ID NO: 185 and as a fragment of the murine WT1 polypeptide as SEQ ID NO: 293 (paragraph 0008 and claim 5 in particular). The '196 publication teaches that immunogenic peptides of WT1 can be formulated into a pharmaceutical composition or vaccine (paragraphs 0109-0111 in particular) that can be used to "prevent, delay or treat a disease associated with WT1 expression" (paragraph 0120 in particular). The aforementioned teachings are disclosed in the parent 09/164,223) application. Applicant should note that, while the front page of

the '196 publication does not refer to the relationship to the '223 application, the first paragraph of the specification does properly claim priority to the '233 application in the first paragraph. The prior art teaching anticipates the claimed invention.

Conclusion

3. The references cited on form PTO-1449 filed on November 5, 2003 have not been considered because copies of the references were not included. While the IDS filed with said form PTO-1449, indicated that copies of the references would be provided at a later date, the copies have not been received in the office. Accordingly, the references have been lined through. However, the references will be considered prior to the next Office Action if they are submitted and the form PTO-1449 marked accordingly. A new copy of the form PTO-1449 and the IDS will NOT be needed.

A copy of the Oka et al. reference noted as reference U1 on form PTO-892 is not included with this Office Action because a copy was submitted by Applicant. The citation thereof on form PTO-892 is merely to make the reference of record.

4. No claim is allowed.

5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571)272-0852. The examiner can normally be reached on M-Th 6:30-4:00; Alternate Fridays 6:30-3:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (571) 272-0841.Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

F. Pierre VanderVegt, Ph.D.
Patent Examiner
January 22, 2004

PATRICK J. NOLAN, PH.D.
PRIMARY EXAMINER
1/28/04